

WHAT IS CLAIMED IS:

1 1. A composition comprising a biologically active compound and a
2 transport moiety, wherein the transport moiety comprises a structure selected from the group
3 consisting of $(\text{ZYZ})_n\text{Z}$, $(\text{ZY})_n\text{Z}$, $(\text{ZYY})_n\text{Z}$ and $(\text{ZYYY})_n\text{Z}$, wherein each Z is L-arginine or D-
4 arginine, and each Y is independently an amino acid that does not comprise an amidino or
5 guanidino moiety, and wherein n is an integer of from 2 to 10.

1 2. The composition according to claim 1, wherein each Y is
2 independently selected from the group consisting of alanine, cysteine, aspartic acid, glutamic
3 acid, phenylalanine, glycine, histidine, isoleucine, lysine, leucine, methionine, asparagine,
4 proline, glutamine, serine, threonine, valine, tryptophan, hydroxyproline, tyrosine, γ -amino
5 butyric acid, β -alanine, sarcosine and ϵ -amino caproic acid.

1 3. The composition according to claim 1, wherein the transport moiety
2 comprises the structure $(\text{ZYZ})_n\text{Z}$, and wherein n is an integer ranging from 2 to 5.

1 4. The composition according to claim 1, wherein the transport moiety
2 comprises the structure $(\text{ZY})_n\text{Z}$, and wherein n is an integer ranging from 4 to 10.

1 5. The composition according to claim 1, wherein the transport moiety
2 comprises the structure $(\text{ZYY})_n\text{Z}$, and wherein n is an integer ranging from 4 to 10.

1 6. The composition according to claim 1, wherein the transport moiety
2 comprises the structure $(\text{ZYYY})_n\text{Z}$, and wherein n is an integer ranging from 4 to 10.

1 7. The composition according to claim 1, wherein the transport moiety is
2 attached to the biologically active compound by a linking moiety to form a conjugate.

1 8. The composition according to claim 1, wherein Y is a gene-encoded
2 amino acid.

1 9. The composition according to claim 1, wherein Y is an amino acid
2 other than a gene-encoded amino acid.

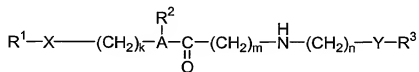
1 10. The composition according to claim 3, wherein each Y is
2 independently selected from the group consisting of glycine, γ -amino butyric acid, β -alanine
3 and ϵ -amino caproic acid, and n is 3 or 4.

11. The composition according to claim 4, wherein each Y is independently selected from the group consisting of glycine, γ -amino butyric acid, β -alanine and ϵ -amino caproic acid, and n is 6, 7 or 8.

12. The composition according to claim 5, wherein each Y is independently selected from the group consisting of glycine, γ -amino butyric acid, β -alanine and ϵ -amino caproic acid, and n is 6, 7 or 8.

13. The composition according to claim 6, wherein each Y is independently selected from the group consisting of glycine, γ -amino butyric acid, β -alanine and ϵ -amino caproic acid, and n is 6, 7 or 8

14. The composition according to claim 7, wherein the conjugate has the following structure:



wherein:

R¹ is the biologically active compound ;

X is a linkage between a functional group on the biologically active compound and a functional group on the linker between R¹ and R³;

Y is a linkage between a functional group on the transport moiety and a functional group on the linker between R¹ and R³;

A is N or CH;

R² is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;

R³ is a transport moiety;

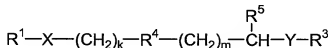
k and m are independently either 1 or 2; and

n is an integer of from 1 to 10.

15. The composition according to claim 14, wherein each of X and Y is independently selected from the group consisting of -C(O)O-, -C(O)NH-, -OC(O)NH-, -S-S-, -C(S)O-, -C(S)NH-, -NHC(O)NH-, -SO₂NH-, -SONH-, phosphate, phosphonate and phosphinate.

16. The composition according to claim 14, wherein each of X and Y is independently selected from the group consisting of -C(O)O-, -C(O)NH-, -OC(O)NH- and -NHC(O)NH-.

17. The composition according to claim 7, wherein the conjugate has the following structure:



wherein:

R¹ is the biologically active compound ;

X is a linkage between a functional group on the biologically active compound and a functional group on the linker between R¹ and R³;

Y is a linkage between a functional group on the transport moiety and a functional group on the linker between R¹ and R³;

R³ is a transport moiety;

R⁴ is S, O, NR⁶ or CR⁷R⁸;

R⁵ is OH, SH or NHR⁶;

R⁶ is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;

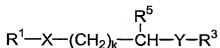
R⁷ and R⁸ are independently hydrogen, alkyl or arylalkyl; and

k and m are independently either 1 or 2.

18. The composition according to claim 17, wherein each of X and Y is independently selected from the group consisting of -C(O)O-, -C(O)NH-, -OC(O)NH-, -S-S-, -C(S)O-, -C(S)NH-, -NHC(O)NH-, -SO₂NH-, -SONH-, phosphate, phosphonate and phosphinate.

19. The composition according to claim 17, wherein each of X and Y is independently selected from the group consisting of -C(O)O-, -C(O)NH-, -OC(O)NH- and -NHC(O)NH-.

20. The composition according to claim 7, wherein the conjugate has the following structure:



wherein:

R¹ is the biologically active compound;

X is a linkage between a functional group on the biologically active compound
and a functional group on the linker between R¹ and R³;

Y is a linkage between a functional group on the transport moiety and a functional
group on the linker between R¹ and R³;

R³ is the transport moiety;

R⁵ is H, OH, SH or NHR⁶;

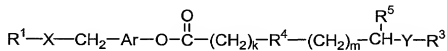
R⁶ is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl; and

k is 1 or 2.

21. The composition according to claim 20, wherein each of X and Y is independently selected from the group consisting of -C(O)O-, -C(O)NH-, -OC(O)NH-, -S-S-, -C(S)O-, -C(S)NH-, -NHC(O)NH-, -SO₂NH-, -SONH-, phosphate, phosphonate and phosphinate.

22. The composition according to claim 20, wherein each of X and Y is independently selected from the group consisting of -C(O)O-, -C(O)NH-, -OC(O)NH- and -NHC(O)NH-.

23. The composition according to claim 7, wherein the conjugate has the following structure:



wherein:

R¹ is the biologically active compound;

X is a linkage between a functional group on the biologically active compound
and a functional group on the linker between R¹ and R³;

Y is a linkage between a functional group on the transport moiety and a functional
group on the linker between R¹ and R³;

Ar is a substituted or unsubstituted aryl group, wherein the methylene and oxygen
substituents are either *ortho* or *para* to one another;

R³ is the transport moiety;

R⁴ is S, O, NR⁶ or CR⁷R⁸;

R⁵ is H, OH, SH, CONHR⁶ or NHR⁶;

R⁶ is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;
R⁷ and R⁸ are independently hydrogen or alkyl; and,
k and m are independently either 1 or 2.

24. The composition according to claim 23, wherein each of X and Y is independently selected from the group consisting of -C(O)O-, -C(O)NH-, -OC(O)NH-, -S-S-, -C(S)O-, -C(S)NH-, -NHC(O)NH-, -SO₂NH-, -SONH-, phosphate, phosphonate and phosphinate.

25. The composition according to claim 23, wherein each of X and Y is independently selected from the group consisting of -C(O)O-, -C(O)NH-, -OC(O)NH- and -NHC(O)NH-.

26. The composition according to claim 12, wherein A is N, R² is benzyl, k, m and n are 1, and X is -C(O)O-.

27. The composition according to claim 13, wherein R⁴ is S, R⁵ is NHR⁶, R⁶ is hydrogen, methyl, allyl, butyl or phenyl, k and m are 1 and X is -C(O)O-.

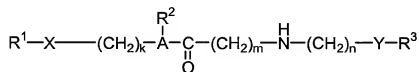
28. The composition according to claim 14, wherein R⁵ is NHR⁶, R⁶ is hydrogen, methyl, allyl, butyl or phenyl, k is 2 and X is -C(O)O-.

29. The composition according to claim 15, wherein Ar is an unsubstituted aryl group, R⁴ is S, R⁵ is NHR⁶, R⁶ is hydrogen, methyl, allyl, butyl or phenyl, k and m are 1 and X is -C(O)O-.

30. A method for increasing the transport of a biologically active compound across a biological membrane comprising:
administering a composition comprising a biologically active compound and a transport moiety, wherein the transport compound comprises a structure selected from the group consisting of (ZYZ)_nZ, (ZY)_nZ, (ZYY)_nZ and (ZYYY)_nZ, wherein Z is L-arginine or D-arginine, and wherein Y is an amino acid that does not comprise an amidino or guanidino moiety, and wherein n is an integer ranging from 2 to 10,
wherein transport of the biologically active compound across the biological membrane is increased relative to transport of the biologically active compound in the absence of said transport moiety.

11
1 31. The method according to claim 20, wherein the biologically active
2 compound is attached to the transport moiety by a linking moiety to form a conjugate.

1 32. The method of claim 21, wherein the conjugate has the following
2 structure:



3
4 wherein:

5 R¹ is the biologically active compound ;

6 X is a linkage between a functional group on the biologically active compound
7 and a functional group on the linker between R¹ and R³;

8 Y is a linkage between a functional group on the transport moiety and a functional
9 group on the linker between R¹ and R³;

10 A is N or CH;

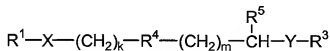
11 R² is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;

12 R³ is a transport moiety;

13 k and m are independently either 1 or 2; and

14 n is an integer of from 1 to 10.

1 33. The method of claim 21, wherein the conjugate has the following
2 structure:



3
4 wherein:

5 R¹ is the biologically active compound ;

6 X is a linkage between a functional group on the biologically active compound
7 and a functional group on the linker between R¹ and R³;

8 Y is a linkage between a functional group on the transport moiety and a functional
9 group on the linker between R¹ and R³;

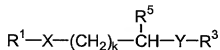
10 R³ is a transport moiety;

11 R⁴ is S, O, NR⁶ or CR⁷R⁸;

12 R⁵ is OH, SH or NHR⁶;

R⁶ is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;
R⁷ and R⁸ are independently hydrogen, alkyl or arylalkyl; and
k and m are independently either 1 or 2.

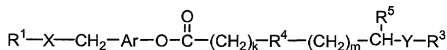
34. The method of claim 21, wherein the conjugate has the following structure:



wherein:

R¹ is the biologically active compound;
X is a linkage between a functional group on the biologically active compound and a functional group on the linker between R¹ and R³;
Y is a linkage between a functional group on the transport moiety and a functional group on the linker between R¹ and R³;
R³ is the transport moiety;
R⁵ is H, OH, SH or NHR⁶;
R⁶ is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl; and
k is 1 or 2.

35. The method of claim 21, wherein the conjugate is of the following structure:



wherein:

R¹ is the biologically active compound;
X is a linkage between a functional group on the biologically active compound and a functional group on the linker between R¹ and R³;
Y is a linkage between a functional group on the transport moiety and a functional group on the linker between R¹ and R³;
Ar is a substituted or unsubstituted aryl group, wherein the methylene and oxygen substituents are either *ortho* or *para* to one another;
R³ is the transport moiety;
R⁴ is S, O, NR⁶ or CR⁷R⁸;
R⁵ is H, OH, SH, CONHR⁶ or NHR⁶;

- 15 R^6 is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;
16 R^7 and R^8 are independently hydrogen or alkyl; and,
17 k and m are independently either 1 or 2.

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